

## Supplementary materials

**Supplemental Table 1. OPA GMT for the two potentially cross-reactive serotypes (6C and 15B) pre- and 30 days post-vaccination, estimated OPA GMT ratios for pre- to 30 days post-vaccination, and the proportions of participants with at least a four-fold rise in OPA GMT at 30 days.**

| Serotype | Endpoint                         | n  | V116<br>(N=51)                              | n  | PPSV23<br>(N=51)                            |
|----------|----------------------------------|----|---|----|---|
|          |                                  |    | Observed response<br>(95% CI <sup>a</sup> ) |    | Observed response<br>(95% CI <sup>a</sup> ) |
| 6C       | GMT (day 1)                      | 51 | 103.87<br>(45.06, 239.45)                   | 51 | 46.51<br>(22.49, 96.20)                     |
|          | GMT (day 30)                     | 51 | 697.66<br>(320.58, 1518.25)                 | 50 | 227.33<br>(107.22, 481.98)                  |
|          | GMFR (day 1–30)                  | 51 | 5.63<br>(3.17, 9.99)                        | 50 | 4.00<br>(2.21, 7.24)                        |
|          | % with 4-fold rise<br>(day 1–30) | 51 | 39.2<br>(25.8, 53.9)                        | 50 | 30.0<br>(17.9, 44.6)                        |
| 15B      | GMT (day 1)                      | 50 | 76.24<br>(39.82, 145.98)                    | 49 | 53.06<br>(29.64, 94.98)                     |
|          | GMT (day 30)                     | 51 | 3049.06<br>(1903.00, 4885.33)               | 51 | 1558.46<br>(980.82, 2476.29)                |
|          | GMFR (day 1–30)                  | 50 | 35.68<br>(18.43, 69.08)                     | 49 | 23.54<br>(13.35, 41.50)                     |
|          | % with 4-fold rise<br>(day 1–30) | 50 | 80.0<br>(66.3, 90.0)                        | 49 | 75.5<br>(61.1, 86.7)                        |

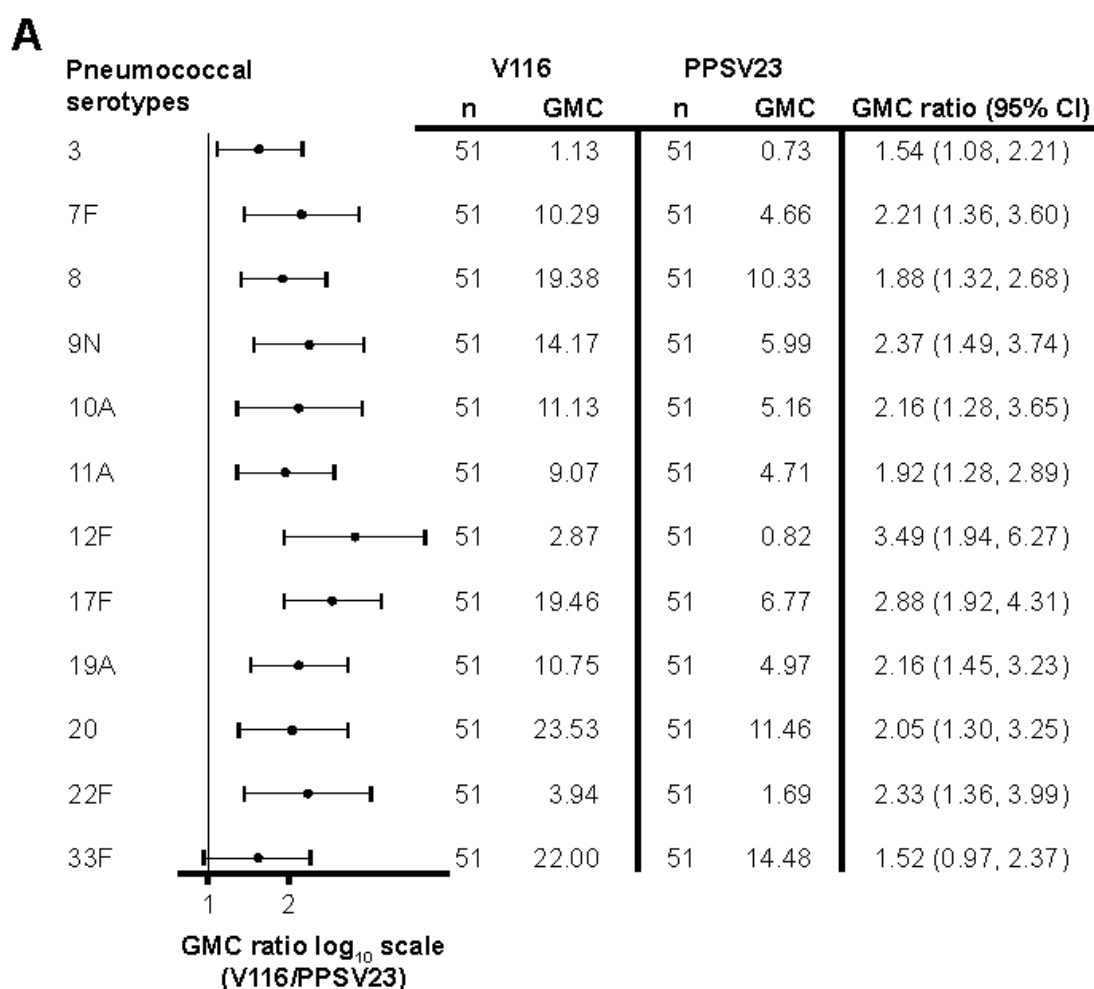
<sup>a</sup>For continuous endpoints, within-group 95% CI were obtained by exponentiating the means of the natural log values based on the t-distribution. For dichotomous endpoints, within-group 95% CI were based on the exact binomial method.

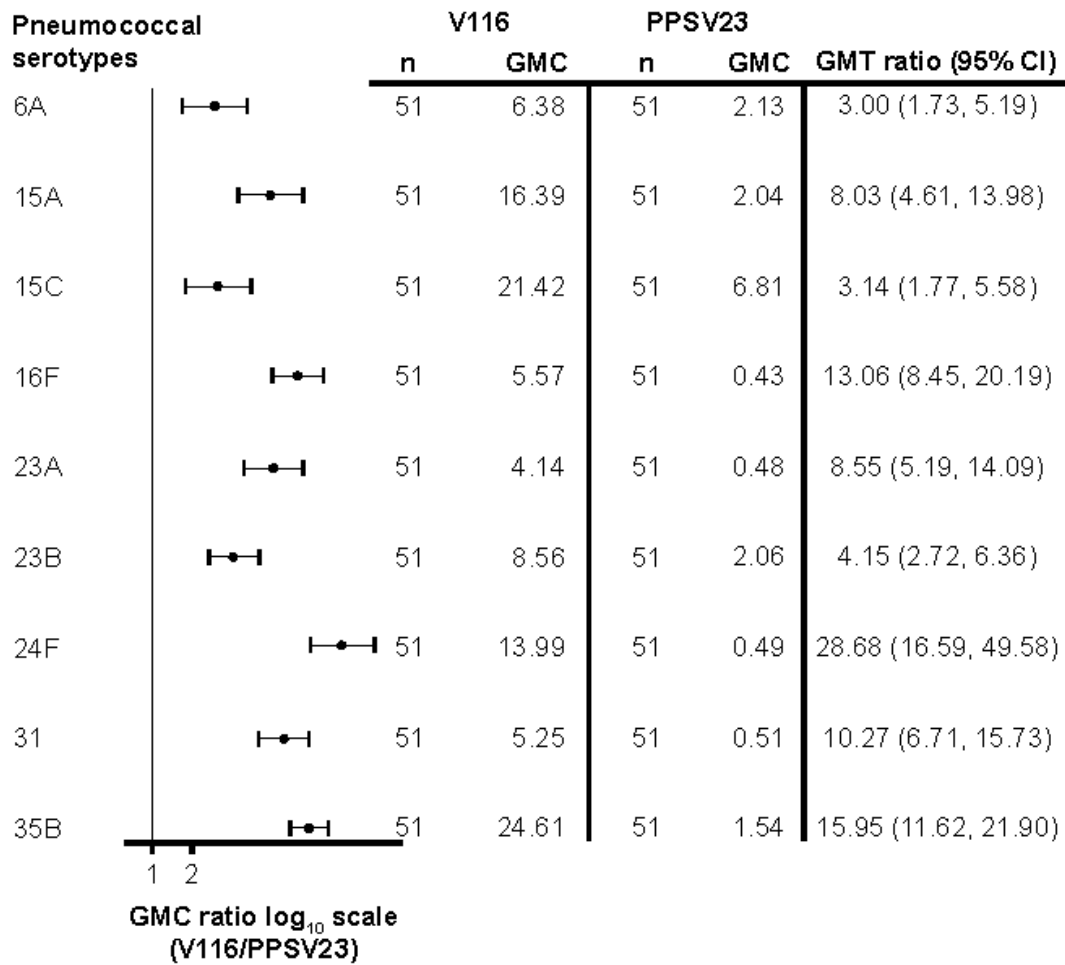
Note: Day 1 is pre-vaccination and day 30 is 30 days post-vaccination

CI: confidence interval; GMFR: geometric mean fold-rise; GMT: geometric mean titer; OPA: opsonophagocytic activity;

PPSV23: 23-valent pneumococcal polysaccharide vaccine; V116: 21-valent pneumococcal conjugate vaccine.

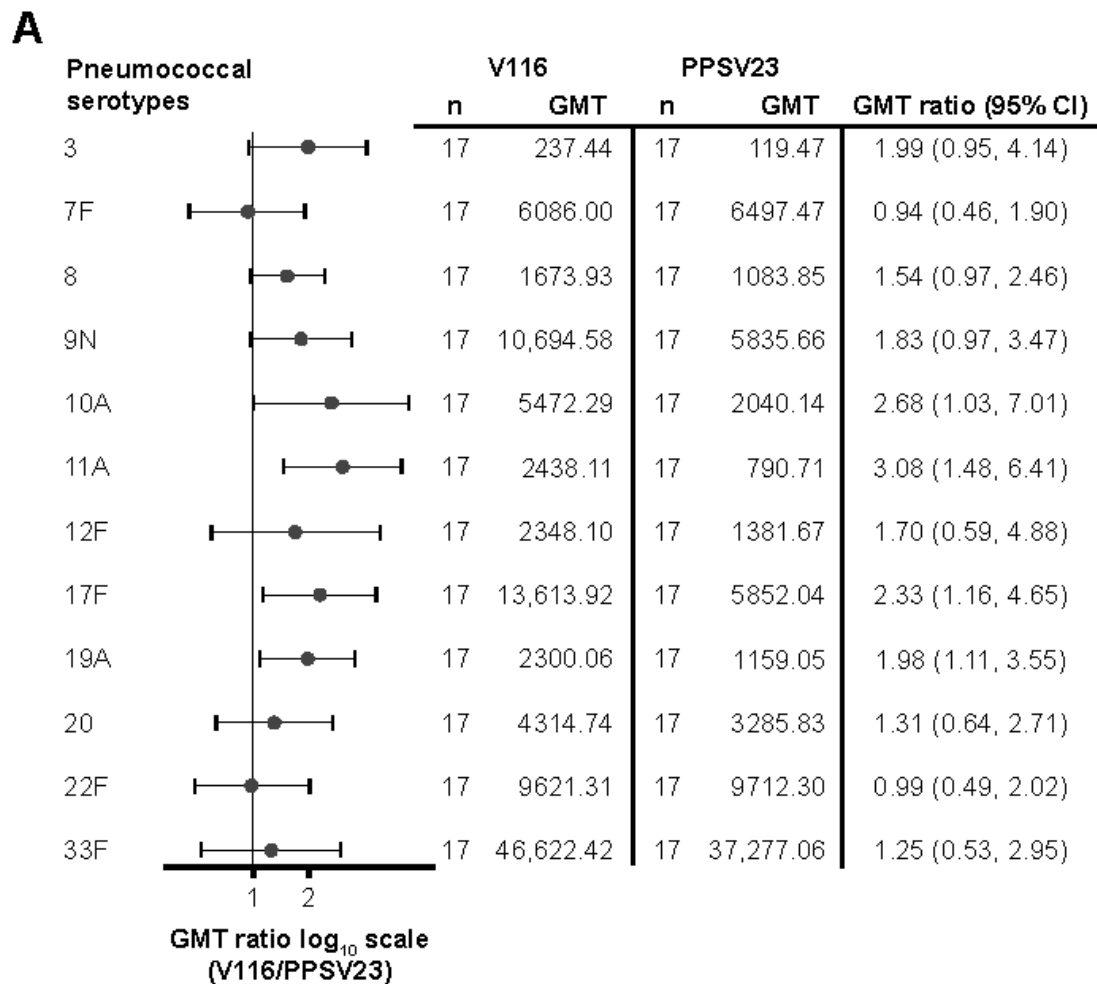
**Supplemental Figure 1. IgG GMC and IgG GMC ratios 30 days after vaccination for (a) the 12 serotypes common to V116 and PPSV23 and (b) the nine serotypes unique to V116.**

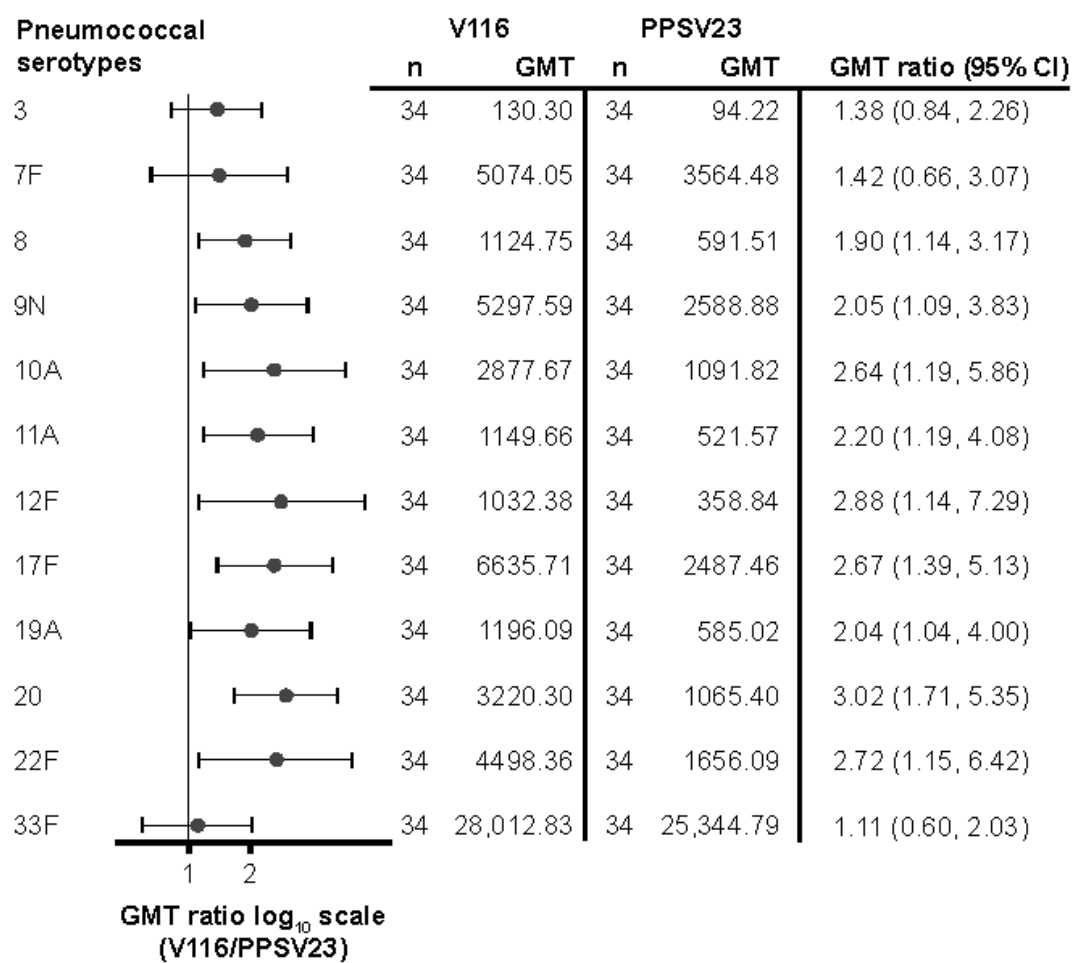


**B**

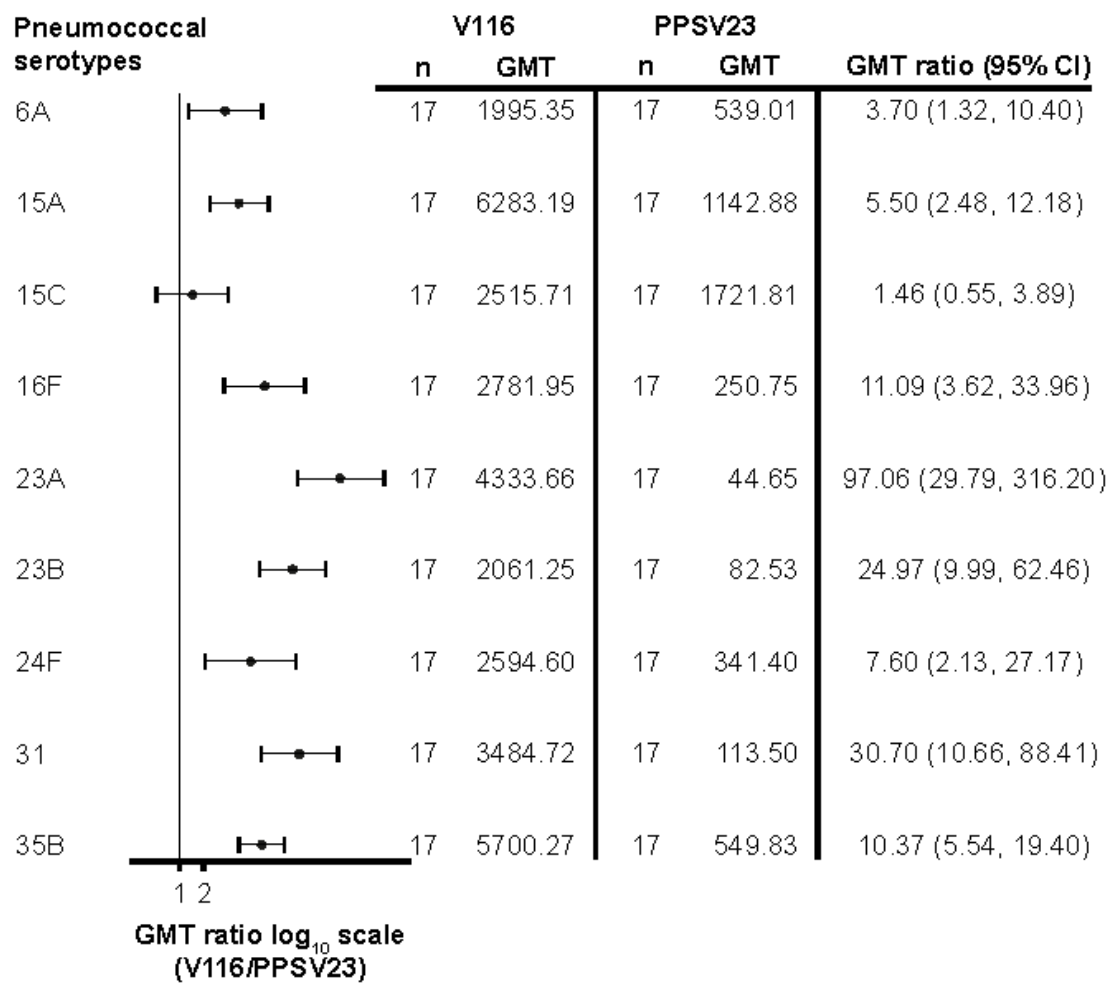
CI: confidence interval; GMC: geometric mean concentration; IgG: immunoglobulin G; PPSV23: 23-valent pneumococcal polysaccharide vaccine; V116: 21-valent pneumococcal conjugate vaccine.

**Supplemental Figure 2. Estimated OPA GMT ratios 30 days after vaccination for the 12 serotypes common to V116 and PPSV23 for those 20 to ≤64 (a) and ≥65 years of age (b) and the nine serotypes unique to V116 for those 20 to ≤64 (c) and ≥65 years of age (d).**

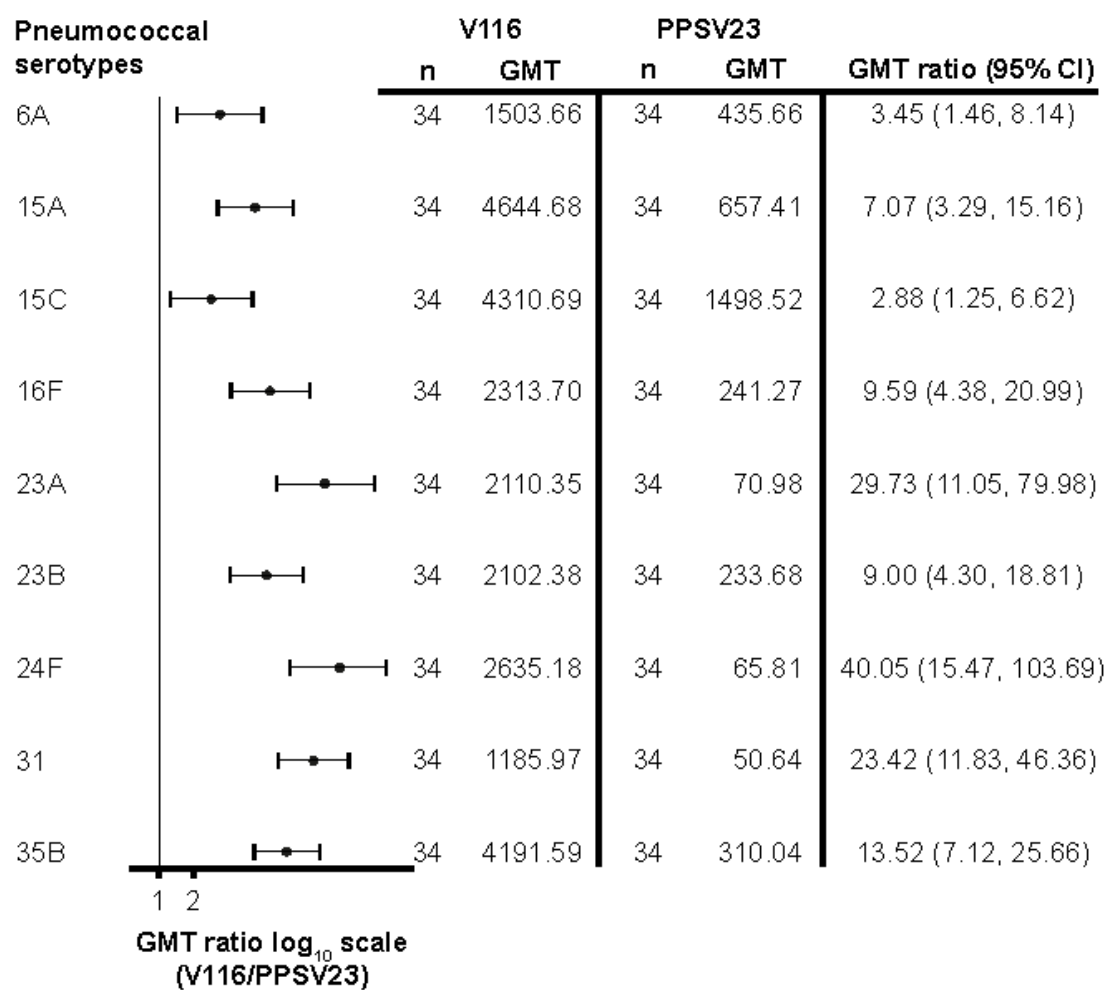


**B**

**C**



**D**



CI: confidence interval; GMT: geometric mean titer; OPA: opsonophagocytic activity; PPSV23: 23-valent pneumococcal polysaccharide vaccine; V116: 21-valent pneumococcal conjugate vaccine.